UNITED STATES DISTRICT COURT
DISTRICT OF MARYLAND

GEORGE CALEB ALEXANDER,
5726 Cross County Blvd.
Baltimore, MD 21209
Baltimore County

Plaintiff,

v.

FOOD AND DRUG ADMINISTRATION,
10903 New Hampshire Ave.
Silver Spring, MD 20993

Defendant.

Civil Action No._____

COMPLAINT

INTRODUCTION

Plaintiff G. Caleb Alexander, by his undersigned attorneys, alleges:

1. This is an action under the Freedom of Information Act ("FOIA"), 5 U.S.C. § 552, *et seq*., for declaratory, injunctive, and other appropriate relief brought by Dr. G. Caleb Alexander, Professor of Epidemiology and Medicine at the Johns Hopkins University Bloomberg School of Public Health.

2. At issue are six FOIA requests Dr. Alexander filed with the Food and Drug Administration ("FDA") more than two and a half years ago. These requests concern the FDA's Risk Evaluation and Mitigation Strategy ("REMS") program, a set of regulatory tools designed to allow the FDA to ensure that the benefits of certain drugs with serious safety concerns outweigh their risks. The REMS program authorizes the FDA to impose a range of specific requirements on dangerous drugs approved for sale, such as mandating that manufacturers provide additional information to patients and medical personnel, requiring prescribing physicians to become certified to prescribe the drug, limiting the administration of the drug to particular types of facilities, or requiring patients to undergo regular lab tests while taking the

drug. Of the approximately 20,000 FDA-approved prescription drugs, only about 60 have REMS requirements.

3. Dr. Alexander, an expert on drug safety, filed his requests in May 2019 to evaluate the FDA's decision to impose, modify, retain, or terminate the REMS for six drugs of particular scientific, regulatory, and clinical interest. In the ensuing two and a half years, the FDA has failed to respond to five of the six requests. Its response to the sixth request was woefully incomplete, and the agency has not acted on Dr. Alexander's administrative appeal filed more than a year ago challenging the adequacy of the agency's search. Throughout, the FDA has provided boilerplate and inconsistent information about when it might respond to Dr. Alexander's requests. The agency's protracted delays have impeded Dr. Alexander from informing the public about the FDA's important regulatory decisions with respect to six drugs with serious safety concerns. These delays violate FOIA, and by this action Dr. Alexander seeks immediate production of all documents responsive to his six requests.

PARTIES

4. Plaintiff Dr. G. Caleb Alexander is a Professor of Epidemiology and Medicine at the Johns Hopkins University Bloomberg School of Public Health. He has authored hundreds of scientific works on the use, safety, and efficacy of various pharmaceutical drugs, sits on numerous editorial and advisory boards, and is frequently invited to speak on best practices and policy relating to pharmaceuticals.

5. Dr. Alexander has successfully advanced public oversight of the REMS program through FOIA disclosures in the past. In 2019, he was the lead author on a paper in the *Journal of the American Medical Association* entitled "Assessment of the FDA Risk Evaluation and

Mitigation Strategy for Transmucosal Intermediate-Release Fentanyl Products."[1] The paper revealed important new facts about the FDA's failure to "require substantive changes to the [REMS] program" for the opioid drugs studied, despite some indication that there was "substantial rates of inappropriate . . . use" by pharmacists, prescribers, and patients.[2] This research garnered national press coverage[3] and led to FDA reform, including the FDA's reformulation of the REMS program governing Transmucosal Immediate Release Fentanyls, the class of opioids examined.

6. Defendant Food and Drug Administration ("FDA") is a component of the Department of Health and Human Services, and is an agency within the meaning of 5 U.S.C. § 552(f)(1).

JURISDICTION AND VENUE

7. This Court has subject-matter jurisdiction over this action and personal jurisdiction over defendant pursuant to 28 U.S.C. § 1331 and 5 U.S.C. § 552(a)(4)(B).

8. Venue is proper under 5 U.S.C. § 552(a)(4)(B).

FACTS

REMS Requirements for the Drugs at Issue

9. Dr. Alexander seeks records relating to the FDA's decision to impose, modify, retain, or terminate REMS requirements for six drugs: zolpidem, prasugrel, mifepristone,

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[1] *See* Jeffrey Eric Rollman, James Heyward, Lily Olson, Peter Lurie, Joshua Sharfstein, and G. Caleb Alexander, *Assessment of the FDA Risk Evaluation and Mitigation Strategy for Transmucosal Immediate-Release Fentanyl Products*, 321 JAMA 676 (2019).

[2] *Id.*, Abstract.

[3] *See, e.g.*, *An FDA program to prevent improper prescriptions of fentanyl had serious, devastating shortcomings* (Feb. 22, 2019, 7:04 PM), https://www.washingtonpost.com/opinions/an-fda-program-to-prevent-improper-prescriptions-of-fentanyl-had-serious-devastating-shortcomings/2019/02/22/4fc906c2-3607-11e9-a400-e481bf264fdc_story.html; Lenny Bernstein, *FDA, drug companies, doctors mishandled use of powerful fentanyl painkiller* (Feb. 19, 2019, 12:29 PM), https://www.washingtonpost.com/national/health-science/fda-drug-companies-doctors-mishandled-use-of-powerful-fentanyl-painkiller/2019/02/19/25106364-343e-11e9-af5b-b51b7ff322e9_story.html.

clopidogrel, salmeterol-fluticasone, and varenicline. The FDA has identified these drugs as presenting exceptional safety risks relative to other FDA-approved drugs.

10. Zolpidem is the scientific name for Zolpimist, marketed by Aytu BioScience, and Edluar, marketed by Meda Pharmaceuticals. The FDA imposed REMS requirements for Zolpimist and Edluar from 2008 to 2011 because some patients had experienced complex sleep-related behaviors and severe, potentially life-threatening allergic reactions to the drugs. As part of the REMS requirements, the FDA required the manufacturers to issue a medication guide for the drugs.[4]

11. Prasugrel is the scientific name for Effient, marketed by Eli Lilly. The FDA imposed REMS requirements for Effient from 2009 to 2012. As part of these requirements, the FDA required a medication guide warning patients of the risk of major bleeding from using Effient. Although the FDA terminated REMS requirements for the drug in 2012, it still required a medication guide for the drug.

12. Mifepristone is the scientific name for Mifeprex, marketed by Danco Laboratories. The FDA imposed some of the most restrictive REMS requirements on Mifeprex in 2011, to which the drug is still subject. Not only did the FDA require a medication guide, but it also required Mifeprex prescribers to meet certain additional qualifications and complete agreement forms before prescribing the drug, and required hospitals and other healthcare

[4] A medication guide is "FDA-approved patient labeling," 21 C.F.R. § 208.3(h), that details—among other information—"the particular serious and significant health concern," 21 C.F.R. § 208.20(b)(2) raised by the drug for which it is required. Medication guides are distributed to patients by manufacturers under FDA regulations, 21 C.F.R. § 208.24(b), and they are issued when "certain information is necessary to prevent serious adverse effects," when "patient decision-making should be informed by information about a known serious side effect with a product," or when "patient adherence to directions for the use of a product are essential to its effectiveness," Medication Guides, Food and Drug Administration, https://www.fda.gov/drugs/drug-safety-and-availability/medication-guides.

facilities to meet certain qualifications before dispensing it. The FDA imposed the REMS because the drug caused a risk of bleeding, infection, and ectopic pregnancy.

13. Clopidogrel is the scientific name for Plavix, marketed by Bristol-Myers Squibb. The FDA imposed REMS requirements for Plavix from February 2011 to May 2011 to mitigate the risk of serious adverse reactions that might result from the combination of Plavix with certain other drugs. The REMS requirements consisted of a Medication Guide and a timetable for submission of assessments of the REMS.

14. Salmeterol-fluticasone is the scientific name for Advair, marketed by GlaxoSmithKline. The FDA imposed REMS requirements for Advair from 2008 to 2012 because the drug posed a risk of pneumonia and asthma-related death. The REMS requirements include a medication guide and box warning.[5]

15. Varenicline is the scientific name for Chantix, marketed by Pfizer. The FDA imposed REMS requirements for Chantix from 2009 to 2016. As part of these requirements, the FDA required a medication guide for the drug. The FDA also required a box warning that alerted physicians to the risk that patients might experience serious neuropsychiatric events from the drug.

Dr. Alexander's FOIA Requests and the FDA's Delays

16. On May 21, 2019, Dr. Alexander submitted six FOIA requests to the FDA seeking records relating to the REMS for the six aforementioned drugs, one request per drug. Each request identified specific documents that were critical to Dr. Alexander's research on the applicable REMS requirements. The requested records include FDA assessments of whether a REMS was needed for the drug, specific items of correspondence between the FDA and the drug

[5] A box warning is a conspicuous warning on the drug's label containing the word "WARNING" in all capital letters that gives a concise explanation of the potential dangers of the drug. *See* 21 C.F.R. § 201.57(c)(1).

manufacturer related to the REMS, REMS assessment reports completed by the manufacturer, and FDA reviews of the REMS reports. True and correct copies of Dr. Alexander's May 21, 2019 FOIA Requests are attached as Exhibits A-F and are incorporated herein by this reference.

17. Dr. Alexander intends to publish the results of his team's analysis of the responsive documents in peer-reviewed medical and public health journals to advance the public's understanding of how the FDA administers the REMS program and how the REMS program could be improved. Dr. Alexander did not file his requests for commercial purposes.

18. The FDA acknowledged receipt of the six requests on May 22 and May 23, 2019.

19. Three months later, in August 2019, Dr. Alexander contacted by telephone the Center for Drug Evaluation and Research ("CDER") FOIA Office—the office within the FDA responsible for processing his requests—regarding the FDA's failure to respond to his requests within 20 business days, as required by FOIA. *See* 5 U.S.C. § 552(a)(6)(A)(i). The CDER FOIA Office told Dr. Alexander that his mifepristone FOIA request was in the fourth or fifth position in the complex queue and that a response might be expected within a matter of weeks or months.

20. A year later, on August 17, 2020 the FDA finally responded to one of Dr. Alexander's requests, his request relating to varenicline. That response, however, failed to provide several documents Dr. Alexander had specifically requested. Missing from the production were, among other documents:

a. "FDA's initial evaluation assessing whether a REMS is needed for varenicline";

b. "the May 2008 FDA letter to Pfizer requiring a REMS and issuing a post marketing requirement for a clinical trial";

c. "[t]he 18-month [MS Assessment] Report submitted [by Pfizer] in or around April 2011";

d. "the 3-year [REMS Assessment] Report submitted [by Pfizer] in or around October 2012";

e. "the 7-year [REMS Assessment] Report submitted [by Pfizer] in or around October 2016";

f. "Pfizer's proposed modifications, including elimination, to the approved REMS plan … including those submitted on November 8, 2013 and September 3, 2014"; and

g. "All FDA reviews of REMS Assessment Reports returned to Pfizer or any other manufacturer of varenicline's."

21. The FDA's cover letter to its August 17, 2020 response to Dr. Alexander's varenicline request did not state that the FDA had withheld any documents in their entirety. A true and correct copy of this letter is attached as Exhibit G.

22. Dr. Alexander promptly filed an administrative appeal of the FDA response to his varenicline request on November 17, 2020, in which he challenged the FDA's failure to perform an adequate search in response to his request and specified the requested documents that the FDA had not produced. A true and correct copy of this appeal is attached as Exhibit H.

23. On November 18, 2020, the FDA acknowledged receipt of Dr. Alexander's appeal to the FDA's determination on his varenicline request. The FDA specified that "[p]ursuant to 5 U.S.C. § 552(a)(6)(B)(i) and 5 U.S.C. § 552(a)(6)(B)(iii) of the FOIA and 45 C.F.R. 5.24(f) of the HHS FOIA regulations, [Dr. Alexander's] appeal falls under the 'unusual circumstances' in that our office will need to consult with another office that has substantial

interest in the determination of the appeal. The actual processing time will depend on the complexity of the issues presented in the appeal." A true and correct copy of this letter is attached as Exhibit I.

24. The FDA told Dr. Alexander on November 20, 2020 that it would "reopen [Dr. Alexander's] request for processing" and asked whether Dr. Alexander would like to "keep [his appeal] open." Dr. Alexander responded on November 22, 2020 that he "would like to continue to keep the appeal [he] ha[s] filed open." A true and correct copy of the November 2020 communications between the FDA and Dr. Alexander is attached as Exhibit J.

25. On February 26, 2021, counsel for Dr. Alexander emailed Sudarshini Satchi, CDER Freedom of Information Branch Chief, to once again bring the delay to the FDA's attention and prompt the FDA to respond to his requests. A true and correct copy of this email is attached as Exhibit K.

26. On March 3, 2021, Guruprasad Udapi, a Supervisory Government Information Specialist at CDER, responded to this email. He said that CDER responds to requests in "date order priority" and that there were approximately 200 FOIA requests with priority over Dr. Alexander's requests. Mr. Udapi also stated that it generally takes 24 months to process requests assigned to the complex queue, like Dr. Alexander's. A true and correct copy of this email is attached as Exhibit L.

27. On March 11, 2021, counsel for Dr. Alexander responded to Mr. Udapi requesting a call to discuss how to resolve the delay in processing Dr. Alexander's requests. A true and correct copy of this email is attached as Exhibit M.

28. Mr. Udapi did not respond.

29. On March 22, 2021, counsel for Dr. Alexander sent an email to Mr. Udapi requesting for the second time a call to discuss how to resolve the delay in processing Dr. Alexander's requests, particularly in light of the FDA's shifting and inconsistent positions on how long it would take to respond to them. A true and correct copy of this email is attached as Exhibit N.

30. Mr. Udapi again did not respond.

31. On April 29, 2021, counsel for Dr. Alexander filed on his behalf an administrative appeal of the FDA's constructive denial of the zolpidem, prasugrel, mifepristone, clopidogrel, and salmeterol-fluticasone requests. A true and correct copy of this administrative appeal is attached as Exhibit O.

32. That same day, the FDA dismissed the appeal as purportedly premature because the FDA had not issued an "adverse determination." A true and correct copy of this dismissal is attached hereto as Exhibit P.

33. Also on April 29, 2021, counsel for Dr. Alexander submitted a letter to the FDA requesting that the agency make a prompt determination on Dr. Alexander's varenicline administrative appeal, which was at that point several months overdue. A true and correct copy of this letter is attached as Exhibit Q.

34. The April 29, 2021 administrative appeal and letter led to a May 5, 2021 phone call between counsel for Dr. Alexander and Mr. Udapi. On this call, Mr. Udapi refused to provide an estimated completion time for Dr. Alexander's requests beyond stating that requests assigned to CDER's complex queue are generally processed within 24 months of receipt – the amount of time that Dr. Alexander's requests had already been pending. Mr. Udapi also indicated that the FDA would not process Dr. Alexander's requests more quickly unless

Dr. Alexander narrowed each request to at most three approval packages for REMS supplements, *i.e.*, communications from the FDA to the drug manufacturer upon the FDA's approval to the manufacturer's proposed modification to a REMS requirement.

35. Three approval packages for REMS supplements is insufficient for Dr. Alexander to effectively evaluate the FDA's handling of REMS requirements for the drugs at issue in his six requests.

36. Dr. Alexander's zolpidem, prasugrel, mifepristone, clopidogrel, and salmeterol-fluticasone requests have been pending for over two and a half years without a response from the FDA.

37. The FDA did not perform an adequate search in response to Dr. Alexander's varenicline request, and Dr. Alexander's varenicline administrative appeal has been pending for over a year without a determination by the FDA.

38. FDA has failed to comply with the applicable time limit provisions of FOIA, and plaintiff has exhausted his administrative remedies. 5 U.S.C. § 552(a)(6)(C)(i).

CLAIMS

FIRST CLAIM FOR RELIEF
(Violation of FOIA for failure to perform an adequate search)

39. Plaintiff repeats, re-alleges, and reincorporates the allegations in the foregoing paragraphs as though fully set forth herein.

40. The FDA failed to make reasonable efforts to search for records responsive to plaintiff's varenicline request in violation of FOIA, 5 U.S.C. § 552(a)(3)(C).

SECOND CLAIM FOR RELIEF
(Violation of FOIA for failure to make records promptly available)

41. The FDA's failure to comply with the statutory time limits for rendering a determination on plaintiff's zolpidem, prasugrel, mifepristone, clopidogrel, and salmeterol-fluticasone requests violates FOIA, 5 U.S.C. §§ 552(a)(6)(A)(i).

42. The FDA's failure to comply with the statutory time limits for rendering a determination on plaintiff's varenicline administrative appeal violates FOIA, 5 U.S.C. §§ 552(a)(6)(A)(ii).

43. The FDA's failure to make promptly available the records sought by plaintiff's requests violates FOIA, 5 U.S.C. § 552(a)(3)(A).

REQUESTED RELIEF

WHEREFORE, plaintiff respectfully requests this Court to:

a) Expedite consideration of this complaint pursuant to 28 U.S.C. § 1657;

b) Declare that the records sought are subject to FOIA and must be disclosed by the FDA in the manner prescribed by FOIA;

c) Declare that Dr. Alexander is entitled to fee waivers.

d) Order the FDA to immediately conduct a thorough search for the records requested by Dr. Alexander;

e) Order the FDA to immediately and expeditiously process the responsive records and produce them to Dr. Alexander;

f) Award Dr. Alexander the cost of this proceeding, including any reasonable attorneys' fees, as expressly permitted by FOIA; and

g) Grant such other and further relief as the Court deems just and proper.

Dated: January 14, 2022

Respectfully submitted,

s/Jennifer DaCosta

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